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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,412	07/11/2001	Shohci Koide	109.050US1	8219

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EXAMINER
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WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/903,412

Applicant(s)

KOIDE, SHOHEI

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 15 July 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) 9-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 51-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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## **DETAILED ACTION**

### ***Status of Claims***

Claims 1-53 are pending in the application

Claims 1-8 and 51-53 are under examination.

Claims 9-50 are withdrawn from consideration as being drawn to non-elected invention, as stated above.

### ***Priority***

In view of the amendment to the specification, priority as claimed is granted.

### ***Information Disclosure Statement***

In view of applicants' statement that the listing of the references at pages 78-89 of the specification relates only to background of the invention, the references have not been considered.

### ***Claim Rejections - 35 USC § 112, second paragraph***

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recited "wherein the stabilizing mutation removes an unfavorable electrostatic interaction in the Fn3". As stated by applicant at page 16 of

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the REMARKS, this phrase relates to a procedure and not to the compound structure of Fn3.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 6, 8 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Koide (WO 98/56915) and Lipovsek for the reasons advanced in the last Office action.

***Response to Arguments***

Applicant argues that Koide does not disclose a fibronectin type III (Fn3) that has a stabilizing mutation rendering the Fn3 molecule more stable than wild type fibronectin.

In response, attention is drawn to page 10, line 30 wherein Koide recites that the mutated polypeptides result in the stabilization of TSAC. See further page 5, line 26 up to page 6, line 10 as to the implicit disclosure of Koide that the Fn3 is stable relative to the disulfide containing Fn3.

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Applicant argues that the procedures for making such a Fn3 molecule with such a stabilizing mutation are also lacking in Koide reference.

In reply, applicant's argument is not commensurate in scope with the claims which also do not recite for any procedure. Nevertheless, said procedure is described by Koide in Example XVI by measuring the pH. It is considered that the procedure of removing an unfavorable electrostatic interaction in the Fn3 that results in a stable Fn3 is inherently taught by Koide. Such unfavorable interactions have to be inherently removed in order for the Fn3 compound to remain stable.

Applicant argues that only mutant Fn3 molecules with reduced stability are disclosed by Koide at Fig.16 and Example XVII.

In reply, Figure 16 as provided in the description, page 14, lines 1-6, does not recite a reduced stability. Example XVI states that Ubi4-K proteins remain comparable to that of the typical globular protein.

Applicant argues that Lipovsek does not disclose a fibronectin type III (Fn3) that has a stabilizing mutation rendering the Fn3 molecule more stable than wild type fibronectin.

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In response, attention is directed to page 19, lines 13-14 of the Lipovsek reference which discloses that the mimics (i.e., mutated antibody) possess stability properties superior to antibodies. See further page 9, line 8 and the relevant sections cited in the last Office action.

Applicant further argues that the procedures for making such a Fn3 molecule with such a stabilizing mutation are also lacking in Lipovsek reference.

In reply, applicant's argument is not commensurate in scope with the claims which also do not recite any procedure. It is considered that the procedure of removing an unfavorable electrostatic interaction in the Fn3 that results in a stable Fn3 is inherently taught by Lipovsek. Such unfavorable interactions have to be inherently removed in order for the Fn3 compound to remain stable.

Applicant argues that both Koide and Lipovsek are limited to a teaching of mutating fibronectin to generate molecules that bind a specific binding partner or target.

In reply, applicant is picking and choosing specific teachings in the prior art to the exclusion of the totality of teaching in the prior art disclosure. Koide clearly teaches the stability of Fn3 as specifically disclosed in Example XVI, which should remain stable when involve in binding activity. Lipovsek

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also clearly discloses that the Fn3 mutant has to be stable relative to the wild type to be physiologically useful.

Applicant argues that Lipovsek discusses different modules of Fn3 (i.e., whole molecules of Fn3) and not individual amino acid positions within an Fn3 molecule.

In response, claim 1 or 51, at least, do not recite for a specific amino acid substitutions. Rather, broadly a Fn3 molecule to which the specific module of Lipovsek is included.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-6, 8 and 51-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Koide(I) or Lipovsek in view of Blaschuk (U.S. 6,391,855) for reasons set forth in the last Office action.

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### ***Response to Arguments***

Applicant argues that the conservative substitution in the Fn3 molecule of Glu with Asp would not remove an unfavorable electrostatic interaction in the Fn3 as in claim 1.

In response, it would be within the ordinary skill in the art to determine whether such substitution affects the stability of the mutant Fn3. It is well known in the art that positively charged residues as Arg or Lys have commonly been substituted for the other charged residues such as Asp or Glu. As disclosed by Koide at page 54, line 5 referring to the Dickinson reference Arg stabilize Fn3. Thus, even without the Blaschuk reference, one having ordinary skill in the art would have known that positively charged residues such as Lys or Arg are known to have stabilizing effect on molecules such as Fn3 as taught by Koide.

### ***Allowable Subject Matter***

Claims 4 and 7 would be allowable if incorporated into claim 1.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 9-50 drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned

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are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
T. D. Wessendorf  
Primary Examiner  
Art Unit 1639

tdw  
September 30, 2003